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Kelly M. McNagny

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BERESKIN AND PARR LLP/S.E.N.C.R.L., s.r.l.

40 KING STREET WEST

BOX 401

TORONTO, ON M5H 3Y2

CANADA

EXAMINER

HALVORSON, MARK

ART UNIT

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/560,103	Applicant(s) MCNAGNY ET AL.	
	Examiner Mark Halvorson	Art Unit 1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 April 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 3,4 and 10-45 is/are pending in the application.
- 4a) Of the above claim(s) 3, 4, 11, 13-33 and 40-45 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 10, 12, and 34-39 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 3, 4 and 10-45 are pending.

Claims 3, 4, 11 and 13-33 have been withdrawn. Claims 40-45 are withdrawn as being drawn to a non-elected invention. Claims 40-45 are drawn to a method of predicting the prognosis of a cancer patient comprising detecting the level of podocalyxin in a sample from a patient and comparing the level of podocalyxin in the sample from the patient wherein an increased level of podocalyxin as compared to the control indicates a poor prognosis. The invention of claims 40-45 is distinct because the patient populations are different and the invention of claims 40-45 would require different method steps. The elected invention is drawn to a method of detecting cancer comprising detecting the levels of podocalyxin and comparing the levels of podocalyxin to a control sample. The control samples of elected invention comprises patients not having cancer. The control group of the invention of claims 40-45 would comprise patients who have cancer and have varying expression levels of podocalyxin. The patients would have to be proactively followed to be able to correlate expression levels with prognosis.

Furthermore, there would be a serious search and examination burden if restriction were not required because the inventions would require a different field of search, the prior art applicable to one invention would not likely be applicable to another invention and the inventions are likely to raise different non-prior art issues under 35 U.S.C. 101 and/or 35 U.S.C. 112, first paragraph.

Should applicant traverse on the ground that the inventions are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

Claims 10, 12, and 34-39 are under examination.

Objections to Specification withdrawn

The objections to the specification are withdrawn in view of Applicant's arguments and the amendments to the Specification and Drawings.

35 USC § 102(b) rejections maintained

The rejection of claims 10, 12, 34-38 and new claim 39 under 35 USC 102(b) as being anticipated by Xu et al. (US Patent No: 6,613, 515, issued Sept 2, 2003, filed Aug 15, 2000, previously cited) is maintained.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The claims are drawn to method of detecting cancer, metastatic cancer or progression of cancer in a patient comprising: (a) determining the level of podocalyxin in a sample from the patient; and comparing the level of podocalyxin in the sample to a control sample, wherein increased levels of podocalyxin and as compared to the control indicates that the patient has cancer, wherein determining the level of podocalyxin comprises determining the amount of nucleic acid molecules, wherein the nucleic acid molecules are mRNA, wherein determining the level of podocalyxin comprises determining the amount of protein using an antibody.

Xu et al discloses that podocalyxin is overexpressed in ovarian carcinoma tissues (Table VI) compared to normal ovarian tissue. Xu et al disclose that podocalyxin mRNA may be detected (column 23, line 52 to column 24, line 27) or

podocalyxin protein may be detected using an antibody (column 31, line 8 to column 32 line 14). Xu et al disclose the detection of podocalysin to measure the progression of cancer. (column 48-49).

Applicants argue that the present application demonstrates that high podocalyxin expression is an independent marker of poor outcome in breast cancer through multi-variant Cox regression analysis. Applicants further argue that they have shown that podocalyxin expression leads to disruption of tight junctions and determination of MCF-7 breast tumor cells, a process that further exemplifies the cancerous effects of podocalyxin. Applicants argue that there is no disclosure or suggestion in Xu et al. that increased expression of podocalyxin in ovarian tumors is indicative of poor outcome or metastasis.

Applicants arguments have been considered but are not persuasive. In response to Applicants arguments that Xu et al does not disclose that increased expression of podocalyxin in ovarian tumors is indicative of poor outcome, it is noted that the features upon which applicant relies are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). The active steps for detecting cancer in the elected claims, including metastatic cancer, comprising measuring expression levels of podocalyxin are disclosed in Xu et al. Xu et al used a cDNA library from metastatic ovarian tumors. (column 55, lines 47-51).

The rejection of claims 10, 12, 35-38 under 35 USC 102(b) as being anticipated by Erlander et al (US Patent Application Publication No: 2004/0002067, published Jan 1, 2004, filed Dec 21, 2001 is maintained.

The claims are drawn to method of detecting cancer, metastatic cancer or progression of cancer in a patient comprising:(a) determining the level of podocalyxin in a sample from the patient; and comparing the level of podocalyxin in the sample to a control sample, wherein increased levels of podocalyxin and as compared to the control

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indicates that the patient has cancer, wherein the cancer is breast cancer, wherein determining the level of podocalyxin comprises determining the amount of nucleic acid molecules, wherein the nucleic acid molecules are mRNA, wherein determining the level of podocalyxin comprises determining the amount of protein using an antibody.

Erlander et al disclose that podocalyxin is upregulated in ductal carcinoma and invasive ductal breast carcinoma compared to patients with normal and hyperplastic breast tissue. (Example VI. Table 5). Erlander et al disclose that podocalyxin is detected by testing for podocalyxin mRNA (paragraphs 10 and 38) and protein using antibodies (paragraphs 39 and 58).

Applicants argue that Table VI of Erlander et al. discloses more than 350 sequences of which podocalyxin is one sequence. Applicants argue that Erlander et al. discriminate between normal/atypical hyperplasia (i.e., non-cancer) and ductal carcinoma in situ and IDC. Applicants argue that there is no differentiation between high and low risk cancer, only between non-cancer and cancer. Applicants further argue that the present application demonstrates that high podocalyxin expression is an independent marker of poor outcome in breast cancer through multi-variant Cox regression analysis. Applicants further argue that they have shown that podocalyxin expression leads to disruption of tight junctions and determination of MCF-7 breast tumor cells, a process that further exemplifies the cancerous effects of podocalyxin. Applicants argue that there is no disclosure or suggestion in Xu et al. that increased expression of podocalyxin in ovarian tumors is indicative of poor outcome or metastasis.

Applicants arguments have been considered but are not persuasive. In response to Applicants arguments that Erlander et al does not disclose that increased expression of podocalyxin in ovarian tumors is indicative of poor outcome, it is noted that the features upon which applicant relies are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26

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USPQ2d 1057 (Fed. Cir. 1993). The active steps for detecting cancer in the elected claims, including metastatic cancer, comprising measuring expression levels of podocalyxin are disclosed in Erlander et al. Erlander et al discloses that expression of podocalyxin is higher in invasive ductal breast carcinoma.

NEW REJECTIONS: based on amendments:

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 12 and 34-38 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for detecting metastatic cancer , does not reasonably provide enablement for a method for determining the risk of metastasis. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The claims are drawn to method of determining whether or not A cancer is metastatic or at risk of metastasis, comprising:(a) detecting the level of podocalyxin in a sample from the patient; and comparing the level of podocalyxin in the sample to a control sample, wherein increased levels of podocalyxin and as compared to the control indicates that the cancer is metastatic.

The specification discloses that podocalyxin is expressed by Invasive Breast Carcinoma. (page 42 line 9 to page 43 line 4). The specification also discloses that increased expression of podocalyxin is correlated with a poor outcome.

One cannot extrapolate the teaching of the specification to the enablement of the claims because the specification does not provide examples or guidance for determining whether higher levels of expression of podocalyxin is correlated with the

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risk of metastasis of a primary tumor. The specification only demonstrates that the podocalyxin is expressed by invasive breast carcinoma and that increased expression of podocalyxin is correlated with a poor outcome. There are no examples demonstrating that the risk of metastasis of a primary tumor is correlated with the expression of podocalyxin. The specification does not provide a nexus between the risk of metastasis and the expression levels of podocalyxin.

Tockman et al (Cancer Res., 1992, 52:2711s-2718s) teach considerations necessary in bringing a cancer biomarker to successful clinical application. Although the reference is drawn to biomarkers for early lung cancer detection, the basic principles taught are clearly applicable to other oncogenic disorders and associated markers such as podocalyxin. Tockman et al teach that prior to the successful application of newly described markers, research must validate the markers against acknowledged disease end points, establish quantitative criteria for marker presence/absence and confirm marker predictive value in prospective population trials (see abstract). Early stage markers of carcinogenesis have clear biological plausibility as markers of preclinical cancer and **if validated** can be used for population screening (p. 2713s, col 1). The reference further teaches that once selected, the sensitivity and specificity of the biomarker must be validated to a known (histology/cytology-confirmed) cancer outcome. The essential element of the validation of an early detection marker is the ability to test the marker on clinical material obtained from subjects monitored in advance of clinical cancer and *link* those marker results with subsequent histological confirmation of disease. This irrefutable link between antecedent marker and subsequent acknowledged disease is the essence of a valid intermediate end point marker (p. 2714, see Biomarker Validation against Acknowledged Disease End Points). Clearly, prior to the successful application of newly described markers, markers must be validated against acknowledged disease end points and the marker predictive value must be confirmed in prospective population trials (p. 2716s, col 2).

Given the disclosure of the specification and the teaching in the art that indicates the requirements for biomarkers that predict an outcome, one skilled in the art could not

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predictably determine the risk of metastasis of a primary tumor by determining the expression of podocalyxin in the cells of the primary tumor.

Therefore, in view of the breadth of the claims, lack of guidance in the specification, the absence of working examples, and the state of the art, it would require undue experimentation for one skilled in the art to practice the invention as broadly claimed.

Claims 12 and 34-38 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. THIS IS A NEW MATTER REJECTION.

The claims are drawn to method of determining whether or not a cancer is at risk of metastasis. There does not appear to be support in the specification as originally filed for a method for determining whether a cancer is at risk for metastasis. Applicants point to page 43 for support of the limitation. However, page 43 discloses that high podocalyxin expression is a marker for poor prognosis and not risk of metastasis. Disclosing where in the specification there is support for this limitation will abrogate this rejection.

Summary

Claims stand rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Halvorson, PhD whose telephone number is (571) 272-6539. The examiner can normally be reached on Monday through Friday from 8:30am to 5 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached at (571) 272-0832. The fax phone number for this Art Unit is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Mark Halvorson
Patent Examiner
571-272-6539

/MISOOK YU/
Primary Examiner, Art Unit 1642